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| 10/516,504 | 12/02/2004 | Hiroyuki Mizuguchi | 081356-0226 | 8630 |

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| EXAMINER |
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MARVICH, MARIA

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1633

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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|------------------------------|--------------------------------------|---|--|
| Office Action Summary | Application No. 10/516,504 | Applicant(s) MIZUGUCHI ET AL. | |
| | Examiner MARIA B. MARVICH | Art Unit 1633 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 5/22/08.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,5-11,13-17 and 19-21 is/are pending in the application.
- 4a) Of the above claim(s) 8-11 and 13-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2,5-7 and 19-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1, 2, 5-11, 13-17 and 19-21 are pending in the instant application. Claims 8-11 and 13-18 are withdrawn from further consideration and therefore, claims 1, 2, 5-7 and 19-21 are under examination.

Claim Objections

Claim 6 is objected to because of the following informalities: claim 6 recites “from which is deleted the E3 region between” whereas it is preferable to recite --wherein the E3 region is deleted from--. Appropriate correction is required.

Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 2 recites that an E1 protein encoded by the E1 region is not expressed or is functionally defective. However, this is an inherent consequence of deleting nucleotides 367 to 2917 or 3375 of Ad35. Deletion of either of these sequences would result in a vector without a functional E1A or E1B (see Table 1, Gao et al).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 5-7 and 19 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Bett et al (2004/0106194; see entire document). **This rejection is maintained for reasons of record in the office action mailed 3/20/08 and restated below.**

The instant claims are drawn to an adenovirus type 35 vector wherein the E1 region is deleted. The instant claims limit the deletion to between 367 and 2,917 or 3,375.

Bett et al teach an Ad35 vector comprising a deletion in the E1 region in which the vector is deficient in E1 as well as deletion in the E3 region (see e.g. ¶¶ 65 and 73-80). A heterologous gene is inserted into the E1 region or the E3 region. The drawings and disclosure teach that the deletion in the E1 region is between 457 and 3402. The purpose of the deletion is to obliterate E1 gene functions. The virus is used to infect target cells.

The instant specification teaches "In particular, the term "E1-deleted region" refers to an E1 protein-encoding region that is functionally defective" (page 6). The sequences were chosen with this purpose in mind and do not appear to provide an advantage over similar deletions. "Specifically, the adenovirus vector according to the present invention may comprise part of the E1 region of the adenovirus type 35 genome as long as the E1 protein that functions in a host cell is not expressed. The "E1-deleted region" may lack all or part of the Ela or Elb region, may lack all of both regions, or may lack a portion that spans both regions, as long as an E1 protein-

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encoding region is functionally defective”. Similarly, the E3 region is deleted in the instant claims to abrogate function of the E3 genes. Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See *in re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). To this end, the deletions of Bett et al are indistinguishable from that of the instant invention.

As well, KSR forecloses the argument that a specific teaching, suggestion or motivation is required to support a finding of obviousness. See the recent Board decision *Exparte Smith* -- USP2d--, slip op. at 20, (BD. Pat. App. & Interfer. June 25, 2007). In light of this, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the vector of Betts et al is indistinguishable from that of the instant claims because Betts teaches that the ad35 vector is deficient in E1 function. As well, it is within the ordinary skill of the art to use available methodologies to isolate a variety of vectors comprising any of a number of deletions that resulting E1 inactivation. One would have been motivated to do so in order as the ability to modify sequences by applying conventional methodologies. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 1, 2, 5-7 and 19-21 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Bett et al (2004/0106194; see entire document) in view of Wadell et al (US 2004/0136958; see entire document). **This rejection is maintained for reasons of record in the office action mailed 3/20/08 and restated below.**

The instant claims are drawn to an adenovirus type 35 vector wherein the E1 region is deleted. The instant claims limit the deletion to between 367 and 2,917 or 3,375 and wherein the virus is used to infect CD34+.

The teachings of Bett et al are as above except neither teaches infection of CD34+ cells.

Wadell et al teach that Ad35 has high affinity to CD34+ cells (see e.g. ¶ 134).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to infect the vector of Betts et al into CD34+ cells as taught by Wadell et al because Betts teaches develop the ad35 vector as a vector for transduction purposes and because Wadell et al teach that Ad35 has high tropism fro CD34+ cells. One would have been motivated to do substitute known vectors using known methods to provide therapeutic vectors to CD34+ cells. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Argument

Applicants' arguments filed 5/22/08 have been fully considered but they are not persuasive. Applicants argue that the instant claims distinguish themselves from the art by reciting deletions that do not remove the pIX promoter from the ad35 vectors. In this case,

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applicants recite vectors in which either nucleotides 367-2917 or 3375 are deleted. However, it is not clear that the resulting vector is distinguishable from the vectors of Betts et al which comprise a deletion of nucleotides 457 to 3401. The art teaches that the E1B 55K gene ends at about amino acid 3400 and the pIX promoter begins at 3488. The art teaches (Havenga et al) that the pIX gene is found from nucleotide 3400 to 4669. This means that the pIX promoters are presumably intact. “Similarly, a prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties (MPEP 2144.05).” Furthermore, the MPEP teaches that optimization of ranges through prior art conditions or through routine experimentation is “The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.” (MPEP 2144.05II). In this case, the choice of deletions seems indistinguishable over one another.

The MPEP (2145) also teaches that “The Hoeksema court further noted that once a prima facie case of obviousness is made by the PTO through citation of references, the burden is on the applicant to produce contrary evidence establishing that the reference being relied on would not enable a skilled artisan to produce the different compounds claimed. *Id.* at 274-75, 158 USPQ at 601. See also *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 295, 297, 227 USPQ 657, 666, 667 (Fed. Cir. 1985) (citing Hoeksema for the proposition above); *In re Grose*, 592 F.2d 1161, 1168, 201 USPQ 57, 63-64 (CCPA 1979) (“One of the assumptions underlying a prima facie obviousness rejection based upon a structural relationship between compounds, such as adjacent homologs, is that a method disclosed for producing one would

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provide those skilled in the art with a method for producing the other... Failure of the prior art to disclose or render obvious a method for making any composition of matter, whether a compound or a mixture of compounds like a zeolite, precludes a conclusion that the composition would have been obvious."). In this case, the vectors are virtually indistinguishable structurally and functionally. The mere differences in nucleotides deleted do not appear to significantly alter the final product and both are the products of routine experimentation. Since, the products are merely variants of one another, one would not conclude that the instant vector requires an inventive step over the prior art.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Maria B Marvich, PhD
Examiner
Art Unit 1633

/Maria B Marvich, PhD/
Primary Examiner, Art Unit 1633